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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,797	07/26/2006	Barbara K. Zehentner-Wilkinson	210121.609USPC	3976

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,797	ZEHENTNER-WILKINSON ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 12/19/2007 is acknowledged and has been entered. Claims 1-4 and 17-26 have been canceled. Claims 5-16 are pending and addressed in this Office action. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The double patenting rejection is withdrawn in view of Applicant's amendment of the claims. The claim rejection under 35 USC 103(a) as being unpatentable over Henderson et al in view of Wang et al and Wang et al and further in view of Edwards and Gibbs is maintained and discussed below.

Claim Rejections - 35 USC § 103

4. Once again, claims 5-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al *(20020172952, Filing date July 2001)* in view Wang et al {Wang et al ('329), herein} (*20020052329, filing date December 2000)* and Wang et al {Wang et al ('012), herein} (*20020099012, filing date June 2001*) and further in view of Edwards and Gibbs (*PCR Methods and Applications, vol. 3, pages S65-S75, 1994*).

Regarding claims 5 and 6, Henderson et al teach a method for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a) detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample (see 0034-0035, 1284-1287, 1295, 1302, 1307, 1321, 1345 and 1349). Henderson further teaches wherein the cancer-associated markers comprise L984P (paragraph 1376, 1382-1390) and L552P (see paragraphs 1493-1495). Henderson also discloses the cDNA sequence for L550S (see 0116), L552 (see 0845) and L984P (see 0930).

Wang et al ('329) teach a method similar to that of Henderson et al for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a) detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung

cancer cells in the biological sample (see 0026-0027; 0504, 0514, 0603, 0616, 0618-0619, 0642, 0644, 0650-0656). Wang et al further teach wherein the cancer-associated markers comprise L762P and L763P (paragraphs 0661 and 0662). Wang et al also teach the cDNA sequence for L762P and L763P (see 0187 and 0189).

Wang et al ('012) teach a method similar to that of Henderson et al and Wang et al ('329) for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a) detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample (see 0026-0027, 0511, 0532-0533, 0763, 0776-0778). Wang et al further teach wherein the cancer-associated markers comprise L587S (paragraph 0805).

The references do not expressly teach wherein two or more cancer-associated markers are detected in the same biological sample. However, methods of detecting multiple targets in a biological sample are well known in the prior art. For example, Edwards and Gibbs teach a method for simultaneously detecting multiple targets using multiplex PCR techniques. Edwards and Gibbs teach that multiplex PCR is a useful tool because it includes internal controls, allows the indication of template quantity and quality, is less expensive in terms of time and reagents, and exhibit great flexibility in experimental design and in overcoming limiting primer kinetics and fragment competition. Therefore, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modify the detection method of Henderson et al and Wang et al ('329) and Wang et al ('012) to encompass steps of multiplex PCR as taught by Edwards and Gibbs for the obvious benefit of simultaneously detecting multiple targets from a single biological sample in a single assay and for the additional advantages taught by Edwards and Gibbs, such as flexibility of experimental design and increase reduction in expense and time that is associated with multiplex PCR.

Regarding claim 7, Henderson et al teach wherein the step (a) comprises detecting the level of mRNA expression using a nucleic acid hybridization technique (see 0034, 1107, 1115 and 1321).

Regarding claims 8 and 9, Henderson et al teach wherein the step (a) comprises detecting the level of mRNA expression using a nucleic acid amplification method selected from the group consisting of PCR, LCR, SDA and NASBA (paragraph 1153).

Regarding claim 10, Wang et al ('329) teach a sequence that is 100% identical to the sequence of SEQ ID NO: 2 (see SEQ ID NO: 161).

Regarding claim 11, Henderson et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 6 (see SEQ ID NO: 789 and Example 1).

Regarding claim 12, Wang et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 26 (see SEQ ID NO: 473).

Regarding claim 13, Henderson et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 4 (see SEQ ID NO: 1871 and Example 9).

Regarding claim 14, Henderson et al teach wherein the cancer is a small cell lung cancer or a non-small cell lung cancer (paragraph 1346).

Regarding claim 15 and 16, Henderson et al teach wherein the biological sample is selected from the group consisting of blood sera, sputum, urine and/or tumor biopsies (1284).

Response to Arguments

5. Applicant traverses the rejection on the following ground: Applicant states that the cited references taken for what they teach as a whole do not teach or suggest the presently claimed method for detecting lung cancer using multiple markers. Applicant states that the references do not teach that the individual markers could be used in combination with any other marker, let alone the markers specifically recited in the claims to better detect cancer. Applicant asserts that nothing in the prior art would

have permitted the person having ordinary skill to reasonably predict that the combination of the individual recited cancer-associated markers would provide the advantages of the presently claimed method. Applicant states that prior to the instant application, it could not be predicted whether the detection of the recited cancer associated markers combined would provide additional benefit over detection of each of them individually. Applicant cites KSR and states that the Courts states that a combination must do more than yield a predictable result. Applicant states that the presently recited combination does more than yield predictable results and is therefore nonobvious.

6. All of the argument have been thoroughly reviewed and considered but are not found persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the combination of references meets the limitation of the claims. The primary reference of Henderson et al in view of Wang et al and Wang et al teach all of the steps of the invention including the each of the cancer associated marker. The references do not teach detecting these markers in a multiplex format. However, this teaching is

disclosed by Edwards and Gibbs and numerous advantages and motivation for wanting to do is provided.

In regards to Applicant's arguments that that the cited prior art did not recognize that the combination of markers could be used to better detect lung cancer, it is noted that Applicant's appears to arguing efficiency of the instant invention when no efficiency has been claimed or supported by the specification. Applicant does not provide sufficient explanation or evidence for this conclusion. MPEP states that "[A] known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994)". In this case, the claims merely recite a method for detecting multiple cancer associated markers, said detection by a multiplex amplification reaction (see Examples in specification beginning at page 28). The cited prior art provides a *prima facie* case for obviousness and a reasonable expectation of success.

In response to Applicant's arguments that a person having ordinary skill would not have reasonably predict the combination of markers for better detecting lung cancer, it is noted that while the claims detect the level of mRNA expression of two or more cancer associated markers, the presence of lung cancer is only recognize if one of the markers is elevated. Thus, contrary to Applicant's arguments, the claims do not require a combination of specific markers be detected in order to advantageously detect lung cancer. Nonetheless, the Examiner respectfully disagrees that one of ordinary skill in the art could not reasonably predict that the combination of the markers would be

advantageous in detecting lung cancer as each of the cancer associated markers were previously known in the art to be effective for detecting lung cancer. The claimed primer sequences were also known in the prior art to detect each of the markers recited therein. Additionally, methods of using multiplex amplification techniques (*the same technique used by Applicant to detect the markers (see Examples*) were widely known and commonly used in the prior art for detecting multiple nucleic acid sequences and combination of sequences that may be associated with cancer. MPEP states, "the fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious." *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). This is particularly true since the cited prior art not only recognized that each of the markers recited therein are effective for screening for lung cancer, but the prior art recognizes that one can screen for multiple markers by using multiplex amplification techniques.

Applicant's arguments are not sufficient to overcome the prior art rejection. Accordingly, the rejections are maintained.

Conclusion

7. No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CBW/

/Gary Benzion/
Supervisory Patent Examiner, Art Unit 1637